# INTERNATIONAL SEARCH REPORT

Int[illegible]onal Application No
PCT/NL2004/000488

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N9/12 C12Q1/48 C12N15/54 C12N5/10 C12P7/64

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C12Q C12P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, Sequence Search, BIOSIS, WPI Data, PAJ, CHEM ABS Data, EMBASE, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 25 April 2005 | 08. 08. 2005 |

| Name and mailing address of the ISA | Authorized officer |
|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax: (+31-70) 340-3016 | Bassias, I |

Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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| P,X | DATABASE Geneseq 'Online! 15 January 2004 (2004-01-15), "Human NOV13a SEQ ID 54." XP002325881 retrieved from EBI accession no. GSN:ADD49081 Database accession no. ADD49081 see sequence -/-- | 1,2,4, 47,48 |

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| P,X | DATABASE Geneseq 'Online! 20 May 2004 (2004-05-20), "Human disease detection and treatment (MDDT) protein - SEQ ID 116." XP002325882 retrieved from EBI accession no. GSN:ADL22667 Database accession no. ADL22667 see sequence | 1,2,4,7, 47,48 |
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| P,X | YAMAOKA SHOHEI ET AL: "Expression cloning of a human cDNA restoring sphingomyelin synthesis and cell growth in sphingomyelin synthase-defective lymphoid cells" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 279, no. 18, 30 April 2004 (2004-04-30), pages 18688-18693, XP002325871 ISSN: 0021-9258 the whole document | 1,2,4, 9-33, 38-63 |
| P,A | LUBERTO CHIARA ET AL: "Purification, characterization, and identification of a sphingomyelin synthase from Pseudomonas aeruginosa. PlcH is a multifunctional enzyme." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 278, no. 35, 29 August 2003 (2003-08-29), pages 32733-32743, XP002325872 ISSN: 0021-9258 | |
| A | LUBERTO CHIARA ET AL: "Sphingomyelin synthase, a potential regulator of intracellular levels of ceramide and diacylglycerol during SV40 transformation: Does sphingomyelin synthase account for the putative phosphatidylcholine-specific phospholipase" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 23, 5 June 1998 (1998-06-05), pages 14550-14559, XP002325873 ISSN: 0021-9258 | |

# INTERNATIONAL SEARCH REPORT

national application No.
PCT/NL2004/000488

**Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 3,5,6,8
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [X] Claims Nos.: 3, 5, 6, 8
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-35, 38-63

**Remark on Protest**

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-35, 38-63

Polypeptides having the requested identity to the motifs as given in claim 1 or to the specific amino acid sequences as given in SEQ ID NOs: 12-22, with the mentioned enzymatic activity as described in claims 9-11, the corresponding nucleic acid sequences encoding said polypeptides, plasmids and microorganisms comprising said nucleic acid sequences processes and uses of the enzymes in question and the thereof produced products, methods for improving the yield of an secretion product in a cell and methods for targeting polypeptides in cellular compartments.

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2. claims: 36, 37

Process to isolate candidates for functional genes of a previously unidentified enzyme with known activity.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Claims Nos.: 3,5,6,8

Claim 1 relates to polypeptides consisting of a sequence which has at least 80% identity to motifs which are defined mainly by variable amino acid residues. Motif (a) for example consists of 7 defined amino acid residues and 53-93 undefined amino acid residues. The requested percentage of identity is not limited to the defined part of the sequence but refers to the complete motif embracing also the undefined part of the motif. Any polypeptide falls into the scope of such a claim, since any amino acid sequence has 80% identity with the undefined part of the motif (and the resulting 20% ?non-identity? with the fixed part of the motif). Consequently, no meaningful search could be performed for such an unclear claim and thus the search for claim 1 was limited to polypeptides having 100% identity to any of the motifs (a) ? (c). Furthermore, it has to be noted that claim 1 comprises numbers within the motifs which are nowhere explained and thus render the true scope of the claim unclear (Article 6 PCT). From the specific sequences 12-22 it could be derived that ?X(35,75)? must mean 35 to 75 variable amino acid residues (?X(8)? means 8 variable amino acid residues). Furthermore, the amino acids given in square brackets '! where interpreted as possible alternatives at this position of the motif. Hence, claim 1 was searched with the above mentioned limitation and the interpretation of the unclear terms as given above.

Claim 3 refers to polypeptides having at least 70% similarity to sequences (SEQ ID NO: 1-11) with about 80% undefined amino acid residues. The requested similarity is not limited to the defined parts of the sequence but refers to the complete sequences, including the undefined sections. Hence any polypeptide having any sequence would fall into the scope of such a claim (see also argumentation given for the limited search of claim 1). Since no clear technical features existed for said claim, no meaningful search was possible.

Claim 5 referring to a polypeptide comprising an amino acid sequence with at least 20% identity to any of the SEQ ID NOs: 12-22 is so broad and thus unclear in the sense of Article 6 PCT. Polypeptides having an identity of only 20% with other polypeptides are not sufficiently supported in the description. Furthermore, it appears not very credible that polypeptides being only 20% identical to each other have the same biological function. If they have different functions, then they solve different technical problems. Due to these discrepancies, no meaningful search could be performed for claim 5.
The same applies for claim 6 and claim 8, since identities of 22% or 30% are also not considered significant.

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Continuation of Box II.2

Claims Nos.: 3, 5, 6, 8

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claim 1 relates to polypeptides consisting of a sequence which has at least 80% identity to motifs which are defined mainly by variable amino acid residues. Motif (a) for example consists of 7 defined amino acid residues and 53-93 undefined amino acid residues. The requested percentage of identity is not limited to the defined part of the sequence but refers to the complete motif embracing also the undefined part of the motif. Any polypeptide falls into the scope of such a claim, since any amino acid sequence has 80% identity with the undefined part of the motif (and the resulting 20% "non-identity" with the fixed part of the motif). Consequently, no meaningful search could be performed for such an unclear claim and thus the search for claim 1 was limited to polypeptides having 100% identity to any of the motifs (a) to (c). Furthermore, it has to be noted that claim 1 comprises numbers within the motifs which are nowhere explained and which render the true scope of the claim unclear (Article 6 PCT). From the specific sequences 12-22 it could be derived that "X(35,75)" must mean 35 to 75 variable amino acid residues ("X(8)" means 8 variable amino acid residues). Furthermore, the amino acids given in square brackets '! where interpreted as possible alternatives at this position of the motif.. Hence, claim 1 was searched with the above mentioned limitation and the interpretation of the unclear terms as given above.

Claim 3 refers to polypeptides having at least 70% similarity to sequences (SEQ ID NO: 1-11) with about 80% undefined amino acid residues. The requested similarity is not limited to the defined parts of the sequence but refers to the complete sequences, including the undefined sections. Hence any polypeptide having any sequence would fall into the scope of such a claim (see also argumentation given for the limited search of claim 1). Since no clear technical features existed for said claim, no meaningful search was possible.

Claim 5 referring to a polypeptide comprising an amino acid sequence with at least 20% identity to any of the SEQ ID NOs: 12-22 is so broad and thus renders the true scope of the claim unclear (Article 6 PCT). Polypeptides having an identity of only 20% with other polypeptides are not sufficiently supported in the description. Furthermore, it appears not very credible that polypeptides being only 20% identical to each other have the same biological function. If they have different functions, then they solve different technical problems. Due to these discrepancies, no meaningful search could be performed for claim 5. The same applies for claim 6 and claim 8, since identities of 22% or 30% are also not considered significant.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

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Int ional Application No
PCT/NL2004/000488

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